Detection of Nonlinear Coupling and its Application to Cardiorespiratory Interaction

Guillermo J. Ortega and Diego A. Golombek

Centro de Estudios e Investigaciones, Universidad Nacional de Quilmes,

R.S. Peña 180, (1876) Bernal, Provincia de Buenos Aires, Argentina

(February 8, 2008)

Abstract

We present here a modification of the Lagrangian measures technique, which allows a reliable detection of interdependency among simultaneous measurements of different variables. This method is applied to a simulated multivariate time series and to a bivariate cardiorespiratory signal. By using this methodology, it is possible to reveal a nonlinear interaction among cardiac and respiration rhythms in pathological conditions.

PACS numbers: 87.22.As, 05.45.+b

The study of natural complex phenomena has urged for the reformulation of signal processing for nonlinear systems. Moreover, with the advent of chaos theory and the "suspicion" that many natural phenomena may behave in a chaotic, although deterministic, way, new analytical methods have been developed. Many of these complex behavior arise as the interaction of the variables involved in the process under consideration. This is especially true in the case of physiological monitoring, where the signals are correlated with one another by feedback mechanisms. Very recently [1] [2], cardiorespiratory interaction has attracted the interest of the nonlinear community as a subject area where application of new methodologies can be tested.

Cardiorespiratory interaction is one of these examples where traditional tools have been used in order to gain information about its underlying dynamics. In this case, an interdependency between heart rate (HR) and respiration (R) rhythms, in physiological conditions, is almost present and is known as Respiratory Sinus Arrhithmia (see [3] and references therein). This phenomenon is especially evident in the usual analysis by means of linear tools, like power spectrum. Accordingly, the power spectrum of the heart rate contains a peak centered at the respiratory frequency [3] [4]. However, there may exist situations where this peak will not be present. This fact is interpreted as a blockade in the interaction between both systems.

In this Letter, we use a recently developed technique [5,6], originally aimed to detect hidden frequencies in time series, with the purpose to demonstrate the interdependence among cardiac and respiratory signals, even in pathological conditions, where traditional tools, like power spectrum, show no signs of interactions. As we will explain below, a simple modification of our original approach will allow us to deal with this rather noisy and short time series. For illustration, we will show the technique in a well known system, the Lorenz system, in order to understand the basic steps.

From the point of view of nonlinear dynamics [7–9], a time series is considered as the "output" or observable of a dynamical system, which can be described by the p-first order differential equation. In the case of chaotic behavior, the system must be necessarily multi-

variate (that is, $p > 2$). Embedding techniques [9] provide a way to reconstruct geometric (attractor structure) and statistical information of the original system by constructing an equivalent representation of it, using time-delayed coordinates. Given a time series of m values, an n-dimensional vector can be constructed:

$$\bar{x_i} = (x_i, x_{i+\tau}, ..., x_{i+(n-1).\tau})$$

where τ is the time delay. In this way, from a single set of observations, multivariate vectors in the reconstructed n-dimensional space are used to trace the orbit of the system.

One of the many ways to describe the dynamics is by studying the long-term behavior of the system. When performing a statistical description of dynamical systems, a central role is played by the natural (or *physical*) probability measure, which describes where the orbit has been, and whose integral over a volume of state space counts the number of points within that volume [7,8]. By performing a partition in the reconstructed phase space of dimension n, this probability density can be estimated as,

$$\hat{\mu}(\mathbf{x}_i) = \frac{n(\mathbf{x}_i)}{\sum_j n(\mathbf{x}_j)} \tag{1}$$

with $n(\mathbf{x}_i)$ equal to the number of points in partition element i around the point $\mathbf{x}_i$. Using this approach, we have recently proposed a new technique to detect hidden frequencies in chaotic time series [5,6]. Here we use an extension of this technique which gives a reliable detection of intrinsic frequencies in noisy and short time series.

Basically, the procedure is the following: for a given time series, a fixed, relatively high embedding dimension is chosen (high enough in order to unfold the geometrical structure of the attractor), and a reconstruction for a given range of time lags τ (the number of lags should be several times the correlation length of the time series) is then performed. For each τ the density of points the trajectory encounters as it evolves is calculated. In this case, the density along the reconstructed trajectory is estimated as

$$\hat{\mu}(\mathbf{x}_i, \tau) = \frac{n(\mathbf{x}_i, \tau)}{\sum_j n(\mathbf{x}_j, \tau)} \tag{2}$$

that is, every $\mathbf{x}_i$ is ordered consecutively along the trajectory. Roughly speaking, this is an estimate of the probability measure the system trajectory encounters as it evolves. In order to estimate the density given by Eq. 1 we have used small spheres around each point $\mathbf{x}_i$, and count the number of other points $\mathbf{x}_j$ inside this volume. Typically, we have used a radius of 5% to 20% of the total extent of the attractor. In this way, a new time series may be constructed with the density data, which now gives information of the different regions in the reconstructed phase space that the system visits. This information reveals recurring motion in the phase space, which is ultimately transferred to the observable time series as periodicity information. A periodogram [10] [11] is performed over this density time series, $\hat{P}$, for each τ (see reference [10] for numerical implementation) as

$$\hat{P}(f_k,\tau) = \frac{1}{N^2}\left[\sum_{j=0}^{N-1} \hat{\mu}(\mathbf{x}_i,\tau) e^{\frac{i2\pi jk}{N}}\right]^2 \tag{3}$$

with N representing the number of data points in the density time series.

In order to plot all the periodograms in a single graph we have used a gray-scale map, and 3 contour curves were superimposed in each plot in order to clarify visual inspection.

A note about the use of the periodogram is in order here. The periodogram is based in the direct Fourier transformation of the signal [11]. If the signal comes from a deterministic system, no further modification is needed in order to the correct interpretation of the periodogram in terms of the Fourier transform. However, in the case of more noise-like signals, it is best to introduce statistical analysis, because for each frequency f_k, $P(f_k)$ is in fact a random variable, which can introduce fluctuations in the estimation process. This is usually accomplished by using *averaging* [11], with several realizations of the estimate. In our case, we have used plain periodograms because in plotting them side by side, several realizations of the periodograms is in fact equivalent to the process of averaging. True frequencies must remain constant in the embedding process, so any kind of fluctuations in the estimate can be readily detected.

The Lorenz system [12] is a model proposed to explain the convective dynamics in the atmosphere (known as the Rayleigh-Benard convection), with the following variables:

$$
\begin{aligned}
\dot{x} &= -sx + sy \\
\dot{y} &= -y + rx - xz \\
\dot{z} &= -bz + xy
\end{aligned}
\tag{4}
$$

and the standard parameters $s = 10.0$, $r = 28.0$ and $b = 2.66$, that yields a chaotic regime. The x coordinate is proportional to the velocity of the circulating flux, while the z coordinate represents the distortion of the temperature with respect to a linear profile between the upper and lower temperature. Figures 1(a) and 1(b) (and first and third stripes in Figure 1(c)) shows the power spectra of the x and z coordinates, which look totally different, forcing the preliminary conclusion that there is no dynamical connection between both phenomena. Moreover, the power spectrum of the x coordinate shows no characteristic frequency at all. Its power is mainly distributed in the lower band; in contrast, the power spectrum of the z coordinate shows a very definite frequency around harmonic number 54. However, both time series belong to the same system. It must be remarked that more involved linear methods, like cross-correlation and coherence gives no further insight in this problem. The above fact reveals the main disadvantage in applying spectral methods for analyzing time series coming from chaotic systems. We have used the x variable as our experimental time series with 2048 data points. An embedding dimension of 3 has been used, and a 10% radius of the attractor was employed in order to estimate the density. The main panel of Figure 1(c) shows the power spectrum of the density time series after applying our method to the x coordinate, for each τ of the embedding process. As the τ parameter varies, the strong frequency which appears in the z coordinate is remarkably recovered, as well as some of the frequencies in the lower band. Inversely, it is also possible to use the z coordinate as the experimental one. Figure 2 shows the same as Figure 1 this time using the z coordinate. Although the power spectrum of this coordinate shows a single sharp peak, perhaps superimposed to a continuous background, our method allows to predict the existence of lower band frequencies in its dynamics. This is evident in the power spectrum of the x or y coordinates.

Two additional points are noteworthy. Some spurious frequencies may appear in this

procedure, for example due to an effect of the finite size of time series. However, these are easily detected because they do not remain constant along the τ scan. By varying the τ parameter in the reconstruction, a nonlinear transformation is performed, and intrinsic properties of the system must remain constant along this procedure, a fact guaranteed by the embedding theorems [9] In fact, we are seeking that $\hat{P}(f_i, \tau) = \hat{P}(f_i)$, independently of the particular τ used. The second point is that intrinsic frequencies (as is the case of harmonic number 54) may disappear for some values of the τ parameter. This is due to the embedding itself, which is only guaranteed to give faithful results in the case of infinitely long data sets and without noise. Some values of the time lag τ may introduce false information, or even hide important frequencies. By performing a scan along a series of τ we can be assured of extracting information of the system itself.

Now, we use our approach in the multivariate time series from heart rate and respiration rhythms. The experiment is fully described in reference [4]. This is a multivariate time series recorded from a patient in the sleep laboratory of the Beth Israel Hospital in Boston. The HR-record is the heart rate, the R-record is the chest volume (respiration force) and the BOC-record is the blood oxygen concentration (measured by ear oximetry). 2048 data points were chosen from the total record, corresponding to the periods of the sleep apnea episodes of the patient. Figure 3 shows the results of applying our analysis to the respiration force time series. We have used an embedding dimension of 4 for the reconstruction process and a radius of the ball of 15% of the reconstructed attractor.

Classical power spectrum analysis of the HR-record shows a strong peak at harmonic number 22 (which corresponds to a frequency of 0.021 Hz). However, the R-record shows several peaks around the harmonic number 260 (0.254 Hz), and no traces of the main frequency of the HR-record. Therefore, it could be concluded that both variables are (linearly) independent. In the original analysis [4], based on standard spectral analysis there is no mention at all of any kind of coupling among both variables in this pathological case, i.e. sleep apnea, contrary to the case of the RSA in the physiological case.

By applying our analysis to the R-record (Figure 3(c), main panel), it appears that the

main frequencies in the reconstructed system are those related with the HR record, and some traces of the original R time series can be observed (around $\tau = 25$). This fact, as in the previous case of the Lorenz system, could be considered as a justification of a nonlinear relation between both variables, and, moreover, suggests that they are related with the same dynamics. However, in this particular case, the flow of information is in the oposite direction as in the case of the RSA.

As in the case of the Lorenz system, we can apply the procedure to the other variable, that is, the HR record (Figure 4). Although some traces of the R record are recovered (specially around $\tau = 90$) almost all of the power is concentrated in the characteristic frequency of the HR. This would imply a very weak coupling from the heart rate to the respiration variable. In the case of the Lorenz system, the equations shows that both variables used, x and z are in fact coupled to each other. That is why it is possible to recover the whole spectrum by using whatever of both variables. One can conclude from the above argument that the coupling among HR and R variables could have a preferential flow direction from the HR to the R, in this pathological condition.

Experience in numerical models shows that hidden frequencies, as detected by our approach, are caused fundamentally by chaotic systems, when one of the variables "fails" in projecting its periodic content over the measured time series. In a linear system, or a nonlinear system without a chaotic behavior, this does not happen. Considering the cardiorrespiratory interaction, the modulation of HR by respiration is clearly seen in the power spectrum of the HR signal under physiological conditions. However, in the pathological condition we are considering, this coupling is not revealed by linear analysis, and moreover, it appears to be in the opposite direction. It could be argued that the underlying dynamics has changed from a linear/nonlinear state to a chaotic behavior. This could be a reason for the dissapearance of the RSA phenomena and the appearance of an inverse coupling. This fact could also be in accordance with the so-called "dynamical diseases" [14] where an abrupt change in the dynamics of the interacting variables is evidenced.

It is very worthy to mention that we have used the data set as it is. No further filter or

smoothing routines have been applied to the data, beyond those of the recording process and to the conversion from the ECG to Heart rate data [4]. We think that it is very important, from the point of view of nonlinear dynamics analysis, to minimize the use of any kind of ”treatment” of the experimental record, which may alter the underlying dynamics, especially in this short and very noisy data sets.

Data requirements for applying this method are almost the same as in any classical spectral analysis. Stationarity [15] of the data is the most important prerequisite, because of the probability estimate that is being calculated. The method is fairly robust against noise contamination, mainly because of the density estimation step, as we have shown with other methods [6,16]. Other than these considerations, the algorithm is of wide use, and could be applied to any kind of experimental data, from biological to geophysical and so on. We are currently applying this analysis to physiological data derived from biological rhythmicity recording in mammals [17]. It should be noted that even more information could be gathered from the reconstructed density time series by applying nonlinear analytical methods [16]. However, the use of power spectra is still the most common tool in time series analysis because of its simplicity and ease of interpretation [10,18], and here we propose to extend its well known capabilities with the aids of nonlinear methods. The most important benefits derived from our methodology might be observed in the case of several variables, where one or more of them are not available experimentally. In this way, more information could be achieved that the one currently available from classical spectral analysis techniques.

The authors are members of CONICET Argentina. Studies in D.A.G.s laboratory are funded by grants from CONICET, UNQ, ANPCyT and Fundación Antorchas.

REFERENCES

[1] C. Schafer, M. Rosenblum, J. Kurths and H. H. Abel, Nature **392** 239 (1998).

[2] C. Schafer, M. Rosenblum, H. H. Abel and J. Kurths, Phys. Rev. E **60**(1) 1 (1999).

[3] S. Akselrod *at al.*, Science **213**, 220 (1981).

[4] D. Rigney, A. L. Goldberger, W. C. Ocasio, Y. Ichimaru, M. G. Moody and R. G. Mark, in *Time Series Prediction: Forecasting the Future and Understanding the Past*, edited by A. S. Weigend and N. A. Gershenfeld, Santa Fe Institute Studies in the Sciences of Complexity, Vol. 15 (Addison-Wesley Publishing Company, 1994).

[5] G. Ortega, Phys. Lett. A **209**, 351 (1995).

[6] G. Ortega, Phys. Rev. Lett. **77**(2), 259 (1996).

[7] H. Abarbanel, R. Brown, J. Sidorowich and L. Tsimring, Rev. Mod. Phys. **65**(4), 1331 (1993).

[8] J.-P. Eckmann and D. Ruelle, Rev. Mod. Phys. **57**(3), 617 (1985).

[9] T. Sauer, J. Yorke and M. Casdagli, J. Stat. Phys. **65**(3/4), 579 (1991).

[10] W.H. Press, S.A. Teukolsky, W.T. Vetterling and B.P. Flannery, *Numerical Recipes* (Cambridge University Press, Cambridge, 1992), 2nd. ed.

[11] A.V. Oppenheim and R.W. Schafer, *Discrete-Time Signal Processing* (Prentice Hall, Englewood Cliffs, New Jersey)

[12] E. Lorenz, J. Atoms. Sci. **20**, 130 (1963).

[13] H. Koepchen, in *Rhythms in Physiological Systems*, edited by H. Haken and H. Koepchen, Springer Verlag Series in Synergetics Vol. 55 (Springer, Berlin, 1991), pp. 3-20.

[14] M. Mackey and L. Glass, *From Clocks to Chaos: The Rhythms of Life*, Ch. 7 (Univ.

Press, Princeton, 1988).

[15] M. Priesley, *Non-linear and Non-stationary Time Series Analysis* (Academic Press, London, 1991)

[16] G. Ortega, and E. Louis, Phys. Rev. Lett. **81** 4345 (1998).

[17] G. Ortega, D. Golombek and L. Romanelli, J. Theoret. Biol. **169**(1) 15 (1994).

[18] R. Bracewell, (1990) Science **248** 697 (1990).

FIGURES

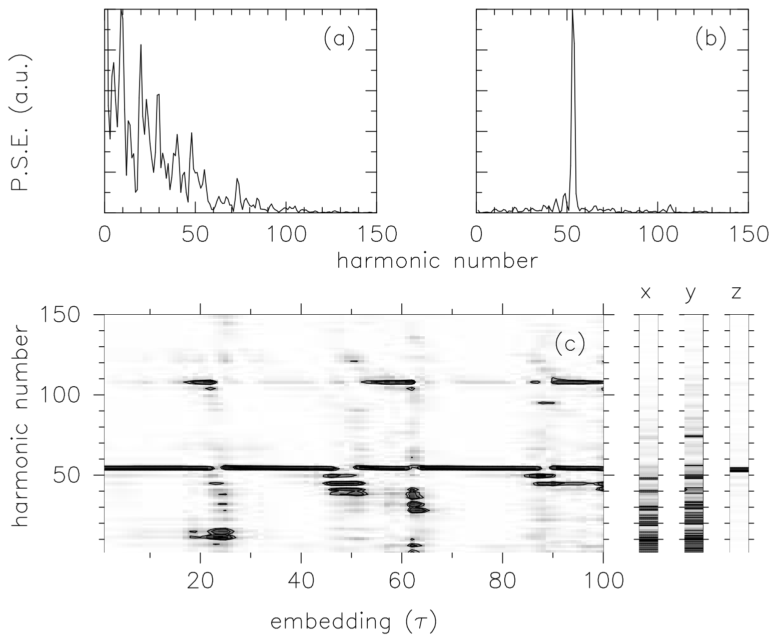

FIG. 1. Spectral analysis and nonlinear coupling in the Lorenz system. Reconstruction using the x coordinate.

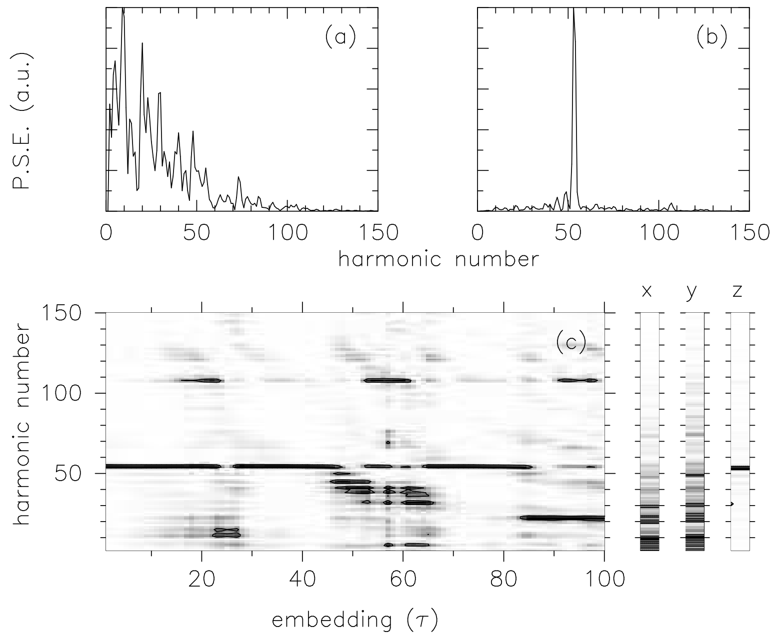

FIG. 2. Spectral analysis and nonlinear coupling in the Lorenz system. Reconstruction using the z coordinate.

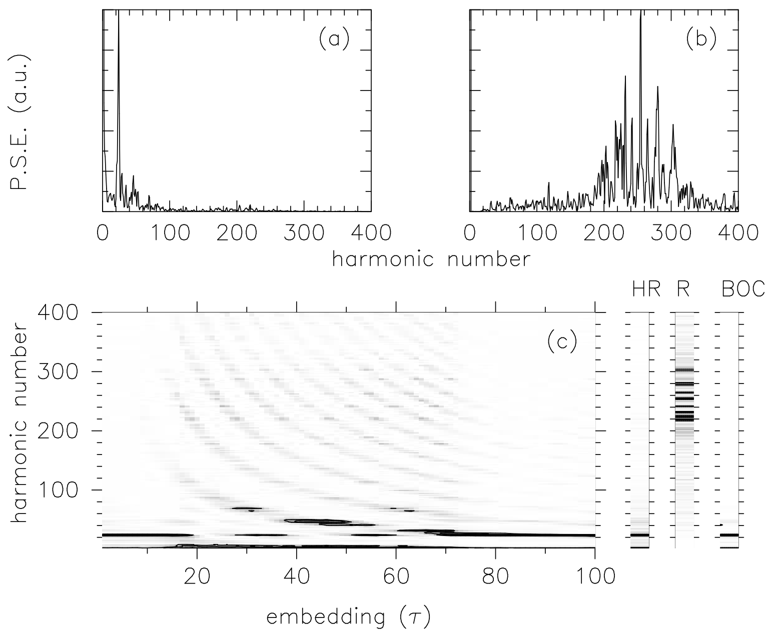

FIG. 3. Spectral analysis and nonlinear coupling in the cardiorrespiratory signals. Reconstruction using the R signal.

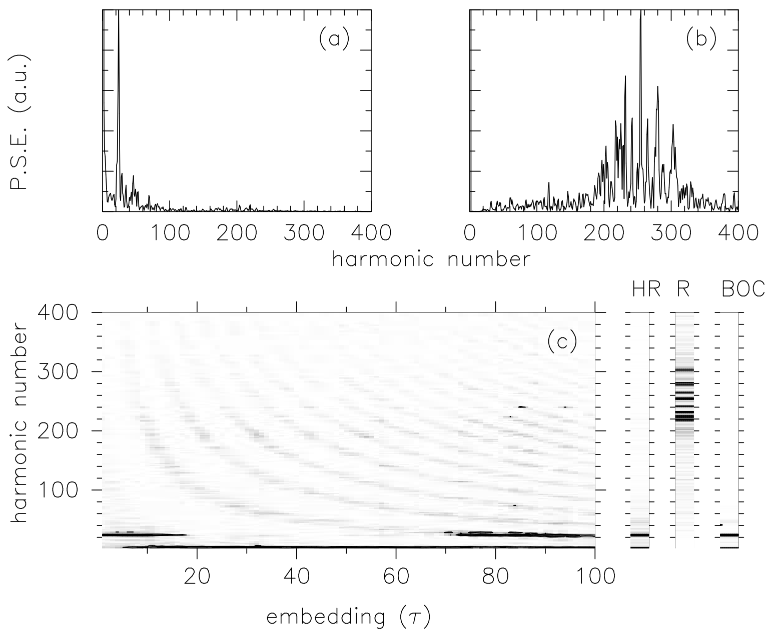

FIG. 4. Spectral analysis and nonlinear coupling in the cardiorrespiratory signals. Reconstruction using the HR signal.